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FILE COVERS 1907 - 4 Jan 2008  VOL 148 ISS 2
FILE LAST UPDATED: 3 Jan 2008  (20080103/ED)
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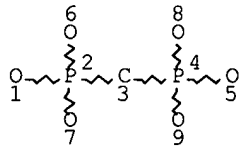

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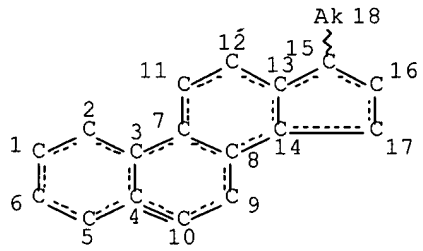

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NUMBER OF NODES IS 18

STEREO ATTRIBUTES: NONE
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L5 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:154640 CAPLUS Full-text
DOCUMENT NUMBER: 146:428048
TITLE: Bone targeting potential of bisphosphonate-targeted liposomes
AUTHOR(S): Hengst, V.; Oussoren, C.; Kissel, T.; Storm, G.
CORPORATE SOURCE: Department of Pharmaceutics, Utrecht Institute for Pharmaceutical Sciences (UIPS), University of Utrecht, 80082, Neth.
SOURCE: International Journal of Pharmaceutics (2007), 331(2), 224-227
CODEN: IJPHDE; ISSN: 0378-5173
PUBLISHER: Elsevier Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The main constituent of bone is hydroxyapatite (HAP). Since HAP is only present in 'hard' tissues like bone and teeth, it represents a promising target for the selective drug delivery to bone. Due to the exceptional affinity of bisphosphonates (BP) for HAP, cholesteryl-trisoxyethylene-bisphosphonic acid (CHOL-TOE-BP), a new tailor-made BP derivative, was used as bone targeting moiety for liposomes. CHOL-TOE-BP-targeted liposomes were designed for the treatment of bone-related diseases to achieve prolonged local exposure to high concns. of the bioactive compds., thereby enhancing therapeutic efficacy and minimizing systemic side effects. The CHOL-TOE-BP-targeted liposomes were characterized regarding particle size and zeta potential. To study the bone targeting potential of these conjugates, an in vitro HAP binding assay was established. The obtained binding data indicate that CHOL-TOE-BP is useful as targeting device for liposomal drug delivery to bone.

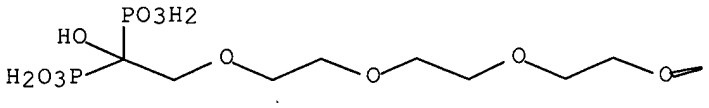
IT 861395-84-8
RL: PEP (Physical, engineering or chemical process); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(bisphosphonate-targeted liposomes bone targeting potential)

RN 861395-84-8 CAPLUS

CN Phosphonic acid, [2-[2-[2-[2-[(3β)-cholest-5-en-3-yloxy]ethoxy]ethoxy]ethoxy]-1-hydroxyethylidene]bis- (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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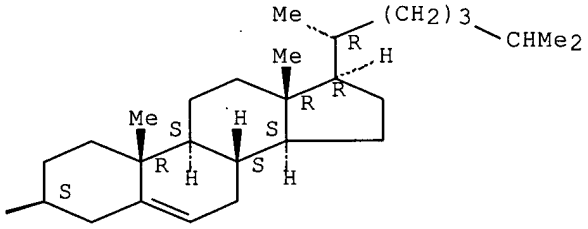

REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:696929 CAPLUS Full-text
DOCUMENT NUMBER: 143:194146
TITLE: Preparation of bisphosphonic acid lipid derivatives
INVENTOR(S): Greb, Wolfgang; Shyhskov, Oleg; Roeschenthaler, Gerd-Volker; Hengst, Verena
PATENT ASSIGNEE(S): MCS Micro Carrier Systems G.m.b.H., Germany
SOURCE: PCT Int. Appl., 28 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

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WO 2005070952	A1	20050804	WO 2005-DE95	20050124
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RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
DE 102004032781	A1	20050811	DE 2004-102004032781	20040706
EP 1706415	A1	20061004	EP 2005-714898	20050124

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, IS

JP 2007518746	T	20070712	JP 2006-549859	20050124
US 2007154537	A1	20070705	US 2006-597059	20060710
PRIORITY APPLN. INFO.:			DE 2004-102004003781A	20040123
			WO 2005-DE95 W	20050124

OTHER SOURCE(S): MARPAT 143:194146

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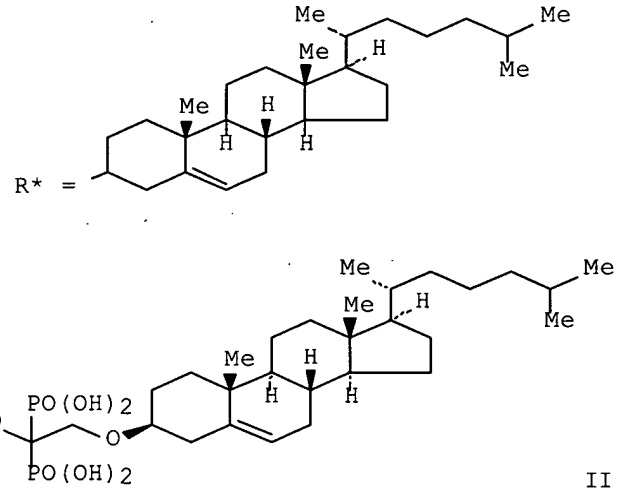


II

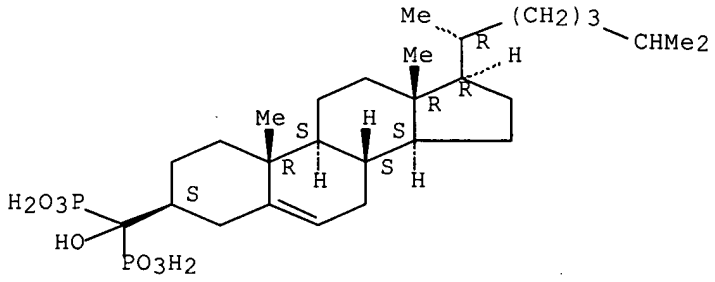
AB Disclosed is a bisphosphonic acid derivative, R1C(XR2)[P(:O)(OH)2]2 [I; R1 = H, OH, C1-6-alkyl, C1-6-alkoxy, C1-6-hydroxyalkyl, C1-6-aminoalkyl, C1-6-haloalkyl; X = bond, C1-20-alkylene, (CH3)m(OCR3HCH2)n(O)o, (CR4HCH2O)p; (CH3)q(OCR 5HCH2)r(O)s(CH3)t; R3 = H, Me; m = 0, 1 - 6; n = 1 - 10, especially 1 - 6; o = 0, 1; R4 = H, CH3; p = 1 to 10, particularly 1 to 6; R5 = H, CH3; q = 0 , 1 to 6; r = 1 to 10, especially 1 to 6; s = 0 or 1; t = 1 to 6; R2 = R*, C8-22-fatty alkyl radical, fatty acid radical], their physiol. acceptable salts and their trimethylsilyl derivs. Thus, cholesteryl-3-hydroxybisphosphonic acid II was prepared from cholesterol, via O-alkylation with BrCH2CO2Li and reaction with P(OSiMe3)3. The inventive compound can be used for producing liposomal prepns. as well as medicaments utilized for the treatment of animals and humans (no data).

IT 861395-80-4P 861395-83-7P 861395-84-8P
861395-85-9P
RL: DGN (Diagnostic use); MOA (Modifier or additive use); SPN (Synthetic preparation); TEM (Technical or engineered material use); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of bisphosphonic acids for liposomal formulations)

RN 861395-80-4 CAPLUS

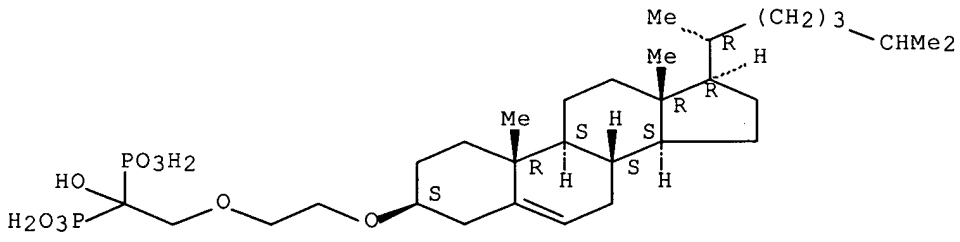
CN Phosphonic acid, [(3β)-cholest-5-en-3-ylhydroxymethylene]bis- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 861395-83-7 CAPLUS
CN Phosphonic acid, [2-[2-[(3β)-cholest-5-en-3-yloxy]ethoxy]-1-hydroxyethylidene]bis- (9CI) (CA INDEX NAME)

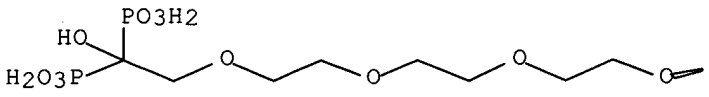
Absolute stereochemistry.



RN 861395-84-8 CAPLUS
CN Phosphonic acid, [2-[2-[2-[2-[(3β)-cholest-5-en-3-yloxy]ethoxy]ethoxy]ethoxy]-1-hydroxyethylidene]bis- (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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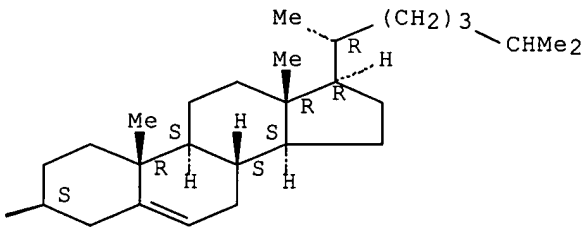
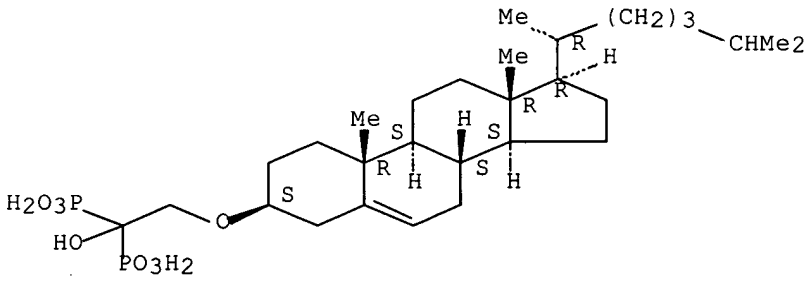


RN 861395-85-9 CAPLUS
CN Phosphonic acid, [2-[(3β)-cholest-5-en-3-yloxy]-1-hydroxyethylidene]bis- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2001:320383 CAPLUS Full-text
DOCUMENT NUMBER: 135:77015
TITLE: Novel Synthesis of Bis(phosphonic acid)-Steroid Conjugates
AUTHOR(S): Page, Philip C. B.; McKenzie, Michael J.; Gallagher, James A.
CORPORATE SOURCE: Department of Chemistry, Loughborough University, Loughborough Leicestershire, LE11 3TU, UK
SOURCE: Journal of Organic Chemistry (2001), 66(11), 3704-3708
CODEN: JOCEAH; ISSN: 0022-3263
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 135:77015
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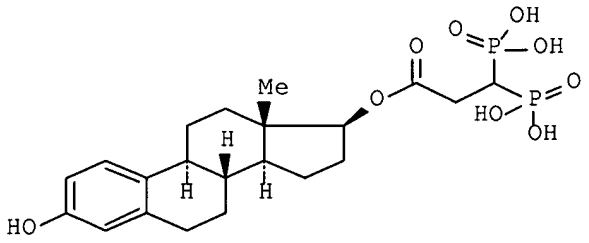

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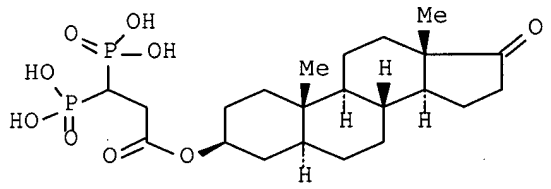


II

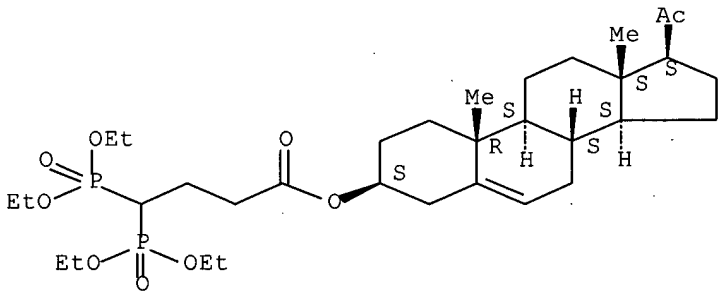
AB An efficient synthesis has been realized for several members of a new class of potential bone resorption inhibitors, e.g. I and II, consisting of steroidal estrogenic units linked at the 3 and 17 positions to a geminal bisphosphonate moiety through an ester linkage of variable length. The convergent synthesis utilizes benzyl bisphosphonates, transesterification, and Meldrum's acid chemical and has the potential to allow many estrogenic derivs. as well as other biol. active compds. to be coupled to the geminal bisphosphonate moiety.

IT 346722-67-6P
RL: SPN (Synthetic preparation); PREP (Preparation)
(novel synthesis of bis(phosphonic acid)-steroid conjugates)

RN 346722-67-6 CAPLUS

CN Pregn-5-en-20-one, 3-[4,4-bis(diethoxyphosphinyl)-1-oxobutoxy]-, (3β)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 71 THERE ARE 71 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1994:31024 CAPLUS Full-text
DOCUMENT NUMBER: 120:31024
TITLE: Preparation of steroid-methylenebis(phosphonate)conjugates as bone resorption inhibitors

INVENTOR(S): Ueno, Hiroaki; Kadowaki, Syuchiro; Kamizono, Akihito; Morioka, Masahiko; Mori, Akihisa
PATENT ASSIGNEE(S): Mitsubishi Kasei Corp., Japan
SOURCE: Eur. Pat. Appl., 55 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 555845	A2	19930818	EP 1993-102143	19930211
EP 555845	A3	19960131		
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JP 05286993	A	19931102	JP 1993-21477	19930209
JP 2746041	B2	19980428		
CA 2089194	A1	19930815	CA 1993-2089194	19930210
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US 5391776	A	19950221	US 1993-15800	19930210

PRIORITY APPLN. INFO.: JP 1992-28497 A 19920214
OTHER SOURCE(S): MARPAT 120:31024
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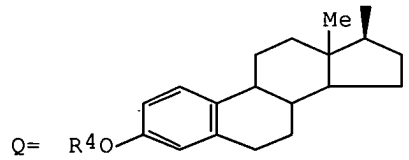


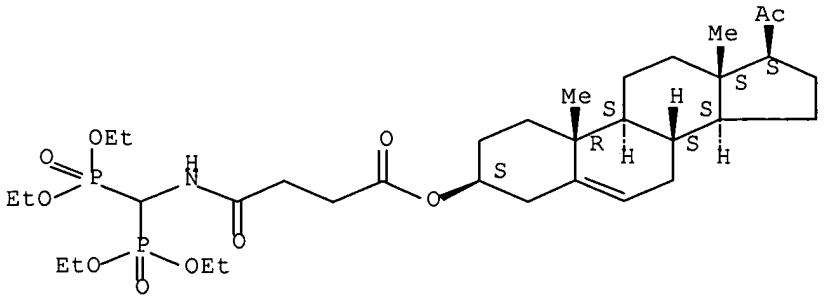
AB R3OACH[P(O)(OR)2]2 [A = CO[NH(CHR1)yYpCO]mNH, COZ1xZqONH, (CH2)kZ2(CH2)l, CO(CH2)n; R = H, alkyl; R1 = H, alkyl, aryl, etc.; R3 = steroid residue; Y, Z = O or NH; Z1 = (substituted) vinylene; Z2 = (cyclo)alkylene, phenylene; l, m, k = 0-5; n = 0-10; p, q, x = 0 or 1; yr = 1-3] were prepared as bone resorption inhibitors. Thus, 17β-hydroxy-3- methoxymethoxy-1,3,5-estratriene was condensed with N,N'- carbonyldiimidazole and the product condensed with H2NCH2CO2Me to give, after saponification, R3O2CNHCH2CO2H (R3 = estratrienyl group Q; R4 = CH2OMe) which was condensed with H2NCH[P(O)(OEt)2]2 to give, after deprotection, R3O2C(NH)9CH2CONHCH[P(O)(OH)2]2 (R3 = Q, R4 = H) (I; q = 1). Similarly prepared I (q = 0) showed significant bone resorption inhibitory action (data given) in ovariectomized rats at 40 μg/kg s.c./day for 28 days.

IT 151869-65-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction of, in preparation of bone resorption inhibitor)

RN 151869-65-7 CAPLUS

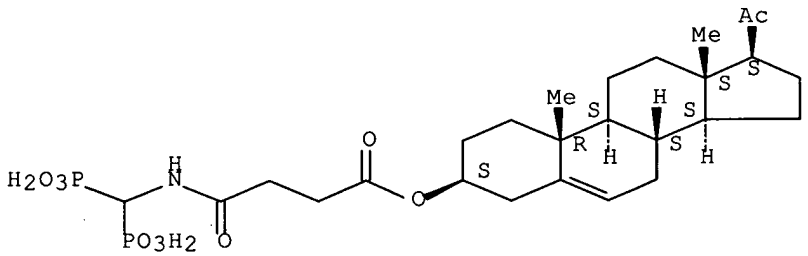
CN Pregn-5-en-20-one, 3-[4-[[bis(diethoxyphosphinyl)methyl]amino]-1,4-dioxobutoxy]-, (3β)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 151869-41-9P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as bone resorption inhibitor)
RN 151869-41-9 CAPLUS
CN Pregn-5-en-20-one, 3-[4-[(diphosphonomethyl)amino]-1,4-dioxobutoxy]-, (3β)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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FILE CONTENT: 1961-PRESENT VOL 148 ISS 1 (20071228/ED)

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MOST RECENT CITATIONS FOR PATENTS FROM MAJOR ISSUING AGENCIES
(COVERAGE TO THESE DATES IS NOT COMPLETE):

US 2007270387 22 NOV 2007
DE 102006046922 15 NOV 2007
EP 1852435 07 NOV 2007
JP 2007299852 15 NOV 2007
WO 2007130704 15 NOV 2007
GB 2437429 24 OCT 2007
FR 2900926 16 NOV 2007
RU 2310676 20 NOV 2007
CA 2584745 13 OCT 2007

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Effective December 15th the iteration and answer limits in MARPAT have increased from 100,000 to 200,000 for both on-line and batch searches. For more information on MARPAT search limits, type HELP SLIMITS at an arrow prompt.

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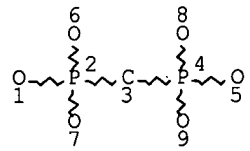

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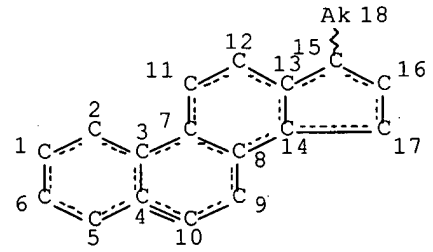

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L7 1173 SEA FILE=MARPAT SSS FUL L1
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L11 2 SEA FILE=MARPAT ABB=ON PLU=ON L10 NOT L5

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L11 ANSWER 1 OF 2 MARPAT COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 134:178396 MARPAT Full-text
TITLE: Synthesis, activity and formulations of pharmaceutical compounds for treatment of oxidative stress and/or endothelial dysfunction
INVENTOR(S): Del Soldato, Piero
PATENT ASSIGNEE(S): Nicox S.A., Fr.
SOURCE: PCT Int. Appl., 94 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

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WO 2001012584	A2	20010222	WO 2000-EP7225	20000727
WO 2001012584	A3	20020829		
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CA 2381409	A1	20010222	CA 2000-2381409	20000727
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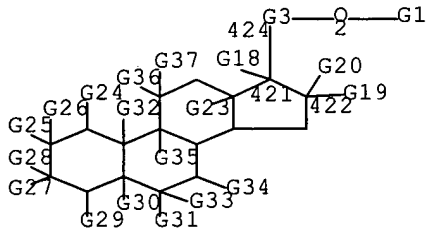
NO 2002000623	A	20020409	NO 2002-623	20020208
MX 2002PA01519	A	20020702	MX 2002-PA1519	20020211
AU 2005202824	A1	20050721	AU 2005-202824	20050628
IN 2006CN01908	A	20070608	IN 2006-CN1908	20060530
KR 760394	B1	20070919	KR 2006-724051	20061116
US 2007197499	A1	20070823	US 2006-642783	20061221
PRIORITY APPLN. INFO.:			IT 1999-MI1817	19990812
			CN 2000-814049	20000727
			EP 2000-953102	20000727
			IN 2002-CN187	20000727
			WO 2000-EP7225	20000727

US 2002-48469 20020207
KR 2002-701883 20020209

AB Compds. or their salts of general formula (I): A-B-N(O)s wherein: s is an integer equal to 1 or 2; A = R-T1-, wherein R is the drug radical and T1 = (CO)t or (X)t', wherein X = O, S, NR1c, R1c is H or a linear or branched alkyl or a free valence, t and t' are integers and equal to zero or 1, with the proviso that t = 1 when t' = 0; t = 0 when t' = 1; B = -TB -X2-O- wherein TB = (CO) when t = 0, TB = X when t' = 0, X being as above defined; X2, bivalent radical, is such that the precursor drug of A and the precursor of B meet resp. the pharmacol. tests described in the description. Synthesis, activity and formulations of pharmaceutical compds. for treatment of oxidative stress and/or endothelial dysfunction are disclosed. The precursors are such as to meet the pharmacol. test reported in the description.

MSTR 1B



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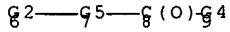

Patent location: claim 1
Note: or salts
Note: additional ring formation also claimed

L11 ANSWER 2 OF 2 MARPAT COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 117:212787 MARPAT Full-text
TITLE: Preparation and formulation of [bis(phosphono)butylaminocarbonyloxy]estratriene and analogs for treatment of bone disease
INVENTOR(S): Saari, Walfred S.; Rodan, Gideon A.; Fisher, Thorsten E.; Anderson, Paul S.
PATENT ASSIGNEE(S): Merck and Co., Inc., USA
SOURCE: Eur. Pat. Appl., 21 pp.
CODEN: EPXXDW

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 496520	A1	19920729	EP 1992-300291	19920114
R: CH, DE, FR, GB, IT, LI, NL				
CA 2059421	A1	19920723	CA 1992-2059421	19920115
JP 04352795	A	19921207	JP 1992-8786	19920122
JP 07035395	B	19950419		
US 5183815	A	19930202	US 1992-839741	19920219
PRIORITY APPLN. INFO.:			US 1991-644178	19910122

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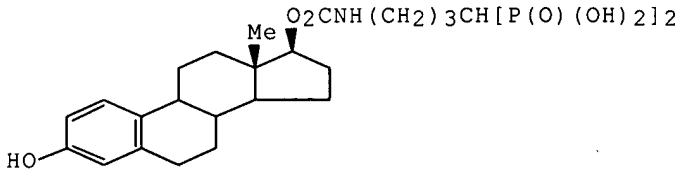
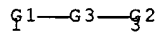


II

AB Compds. ABC [A = residue of a hydroxy-containing steroidal hormone having human bone resorption-antagonist activity or bone formation-stimulatory activity; C = residue of an amino- or hydroxyalkyl-1,1-bis(phosphonate) having human bone affinity; B = covalent linkage connecting A through the hydroxyl moiety and C through the amino or hydroxyl moiety, which linkage can hydrolyze in the human body in the vicinity of bone to release steroidal hormone A] were prepared for treatment of bone disorders (no data). Thus, [(Me2CHO)2P(O)]2CHR (I; R = H), was condensed with CH2:CHCN and the product hydrogenated to give I [R = (CH2)3NH2], which was condensed with 3-benzyloxy-17β-chlorocarbonyloxyestra-1,3,5(10)- triene (preparation given) to give, after deprotection, title compound II.

MSTR 1A



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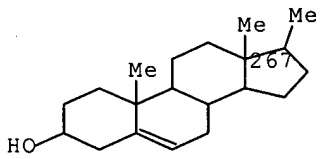

Derivative: and pharmaceutically acceptable salts or esters
Patent location: claim 1

MSTR 1B

G1—G3—G2
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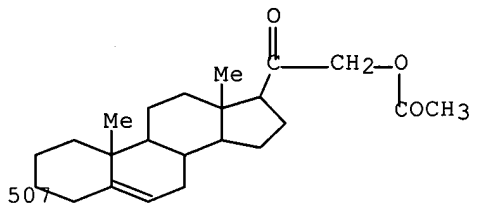

Derivative: and pharmaceutically acceptable salts or esters
Patent location: claim 1

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